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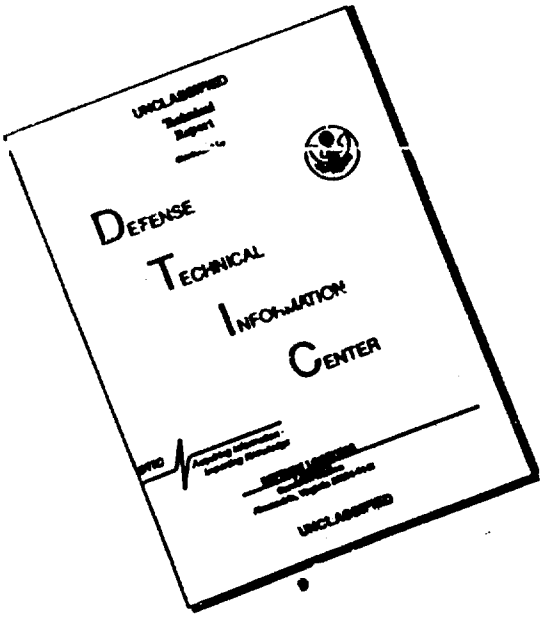

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TRANSLATION NO. 82

DATE: Sept 1968

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

Problems of Virology, USSR, No. 2, 1956, Pages 32-37

Etiology of Raging Disease of Animals in the Arctic (diseases resembling rabies)

Report 1. Biological Characteristics of Raging Virus, by R. A. Kantorovich (Virological Laboratory of the Archangelsk Scientific-Research Institute of Epidemiology, Microbiology and Hygiene)

The problem of raging disease is one of the little-studied problems of the regional pathology of the North.

The term raging (dykovania or dykost) has for some time meant a special illness of wild and domestic animals and is encountered in various areas of the Arctic. According to data in literature and vocal reports of hunters, travelers and local residents, this disease is noted most often among the polar fox and fox, but is also observed among the wolf, reindeer and other animals.

The illness manifests itself basically in the behavior of the animals; ordinarily shy or timid, the polar fox and fox, becoming infected with raging disease, lose all sense of fear, often enter populated areas and fall upon domestic animals (mainly dogs) usually biting them. There have been noted, though rarely, instances where they bit people. The dogs, 2-3 weeks after contacting the bite of the raging animals, develop a disease which closely resembles rabies by clinical features and means of transmission.

At the present time there are significant differences in the treatment of this illness by medical and veterinary personnel and by workers of the fur trade. In numerous manuals on fur trading, raging disease is without special basis, identified with encephalomyelitis of the fox and polar fox. Veterinarians interpret it as rabies. Medical workers have contacts yearly with people who have been bitten by raging dogs which requires production of urgent prophylactic measures.

The actuality of the given problem for medical workers of the North is what stirred us to initiate studies in 1853 for clarification of the nature of raging disease and its relationship to other neurovirus infections. The literature gives only single reports on the experimental study of the etiology of this disease (2, 3). Detailed studies of the characteristics of the agent of raging disease and its interrelationship to other neurovirus agents and analysis of its pathomorphological variations have not been studied up to this time.

This publisheddmaterial expresses the results of a many-sided study of two strains isolated in 1954 from ailing animals.

The origin of one of the isolated strains (Ness) is a fox which was killed while infected with raging disease in one of the areas of the Arctic.

During dissecting of the animals we discovered hyperemia of the brain tissue and infection of the urinary bladder. In the lungs, liver and kidneys there were no pathological variations. A 10% suspension of the brain of the fox on a beef-peptone bouillon was introduced intracerebrally to 2 rabbits and 6 mice (Graph 1).

On the 11th and 12th days after infection 3 mice showed signs characteristic for the illness; shivering and disruption of movement coordinations. Acute hyperesthesia was noted later, also convulsions and infection of the rear extremities followed quickly by death. The illness, as a rule, did not last more than 1-2 days.

Three mice, in which the symptoms of the illness did not appear, were killed on the 11th day; a 10% suspension was prepared from their brains and introduced into a new series of mice. All the mice of the first passage fell on the 8-12th day after infection.

The infected rabbits became ill; the length of the incubation period was 14-17 days. The illness was indicated by shaking of the head, convulsions of the neck and masticatory muscles, disruption of coordination, infection of front and/or rear extremities; 2-3 days after the start of the illness all the animals died. During dissecting of the dead animals there was observed, as a rule, hyperemia of the brain tissue and infection of the sphincter of the urinary bladder. Sowing of the brain suspension on various nutritive mediums gave negative results.

During passage of the brain tissue of the dead animals in newly infected mice and rabbits analogical illnesses appeared. On the 5th and 6th passages of the material being tested there was noted a shortening of the incubation period to 7-8 days. During this the clinical signs remained as before.

The other strain of virus of raging disease (pyosha) also was isolated from a fox which had signs of illness and located near the area center of Pesha (Pyosha).

As can be seen on the drawing, the infection of the experimental animals with a 10% suspension of the brain of the fox, in all cases, was succeeded by illness which appeared after 14-17 days incubation. The illness was characterized by those same signs which were noted during infection with the strain Ness. One can only point out the great frequency of infection of the front and rear extremities which were often replaced by characteristic paralysis of respective groups of muscles. Further passages of the infection material caused analogical illnesses in the infected animals.

Thus, during the very first passages there were isolated 2 strains of an unknown nature in the process of our studies. Study of the characteristics of the isolated agent was started with tests of filtration of a 5% suspension of

brain through 'rublevsk' filters No. 1, 2, 3 and 12.

The original material (control line) and the obtained filtrates were tested for presence of virus by intracerebral infection of white mice.

The obtained filtrates possessed an expressed pathogenic activity (Table 1) which confirms the virus nature of the isolated strain.

Further on we studied the pathogenic characteristics of the virus of raging disease. The pathogenic activity of a 10% suspension of virus was studied for various types of laboratory animals. Virus of the 1st and 2d passages were used in the tests.

The intracerebral method of infection was the most effective, less so - intramuscular and even less - subcutaneous method of infection. The advantages of the intracerebral method of infection are also confirmed by the data of Table 3, as it shows that the intracerebral method by far excells the intramuscular or subcutaneous methods according to effectiveness; with the latter, death of the mice takes place only in those cases where a concentration of the virus suspension (10-1) is used.

Because a majority of the neurovirus agents are distinguished by a high stability to action of glycerine, we became interested in studying the rate of survival of the isolated viruses during storage of them in 50% glycerine on ice.

Virus-incorporated brain material was heldin the above conditions for periods of 2, 4, 7 and 9 months after which 10% suspensions were prepared and introduced to white mice (Table 4).

Thus, the pathogenic activity of the strains fully remained during the 2-4 month storage, in later periods it gradually decreased.

The stability of the virus of raging disease was also studied in regard to the action of weak solutions of phenol.

A 5% virus suspension in a physiological solution containing 1% phenol was held at 2-4°C and tested at various periods for presence of live virus by means of intracerebral infection of white mice (Table 5).

As Table 5 indicates, the studied strains retained their pathogenic characteristics during storage in 1% phenol for 1-2 months after which their activity sharply decreased. The reaction of the virus of raging disease to the phenol relates it with the virus of rabies which, as is known, is distinguished by a high stability to the action of weak solutions of this substance.

To study the action of ultraviolet rays on the virus, a 10% suspension of brain was exposed to a mercury-quartz lamp PRK-4 at a distance of 30 cm, and during study of the effect of temperatures it was subjected to a water bath. The thus exposed material was injected into white mice (Tables 6 and 7).

Thus, under the action of the ultraviolet rays the pathogenic activity of the virus suspension is quickly lost.

The pathogenic activity is retained only at 50°C. Heating at 55 and 60°C quickly inactivates the virus.

As can be seen from the data set forth here, the isolated strains of raging virus possess characteristics common with numerous neurovirus agents, but their susceptibility to action of high temperatures distinguishes them from virus of demyelinizing encephalides which possess significant stability to the said actions. According to clinical symptoms during actual and experimental infection and reactions to the action of weak solution of phenol the studied strains are related to the agent of rabies.

CONCLUSIONS

1. During virological analysis of foxes with raging disease we isolated 2 strains of virus.

2. The strains proved pathogenic for various types of laboratory animals and caused an illness in the latter with signs of infection of the central nervous system.

3. The virus of raging disease displayed a high stability to storage in glycerine and 1% phenol and was quickly inactivated during action of high temperatures and ultraviolet irradiation.

4. The biological characteristics of the viruses of raging disease - specter of pathogenicity, course of experimental infection, behavior to numerous physical and chemical factors - are related to the studied strains of other neurovirus agents and partially to virus of rabies.

Literature

1. Formozov, A. N. Fluctuations of the number of commercial fur animals, M., 1935. 2. Truevich, E. I. and Tebyakina, A. E. J. Micro., Epidem., and Immunol., 1947, No. 2, p.17-25. 3. Shcherstoboev, K. N. In book: Works of the Irkutsk Scientific-Research Veterinary Experimental Station, b.1, p.99-116, Irkutsk, 1949.

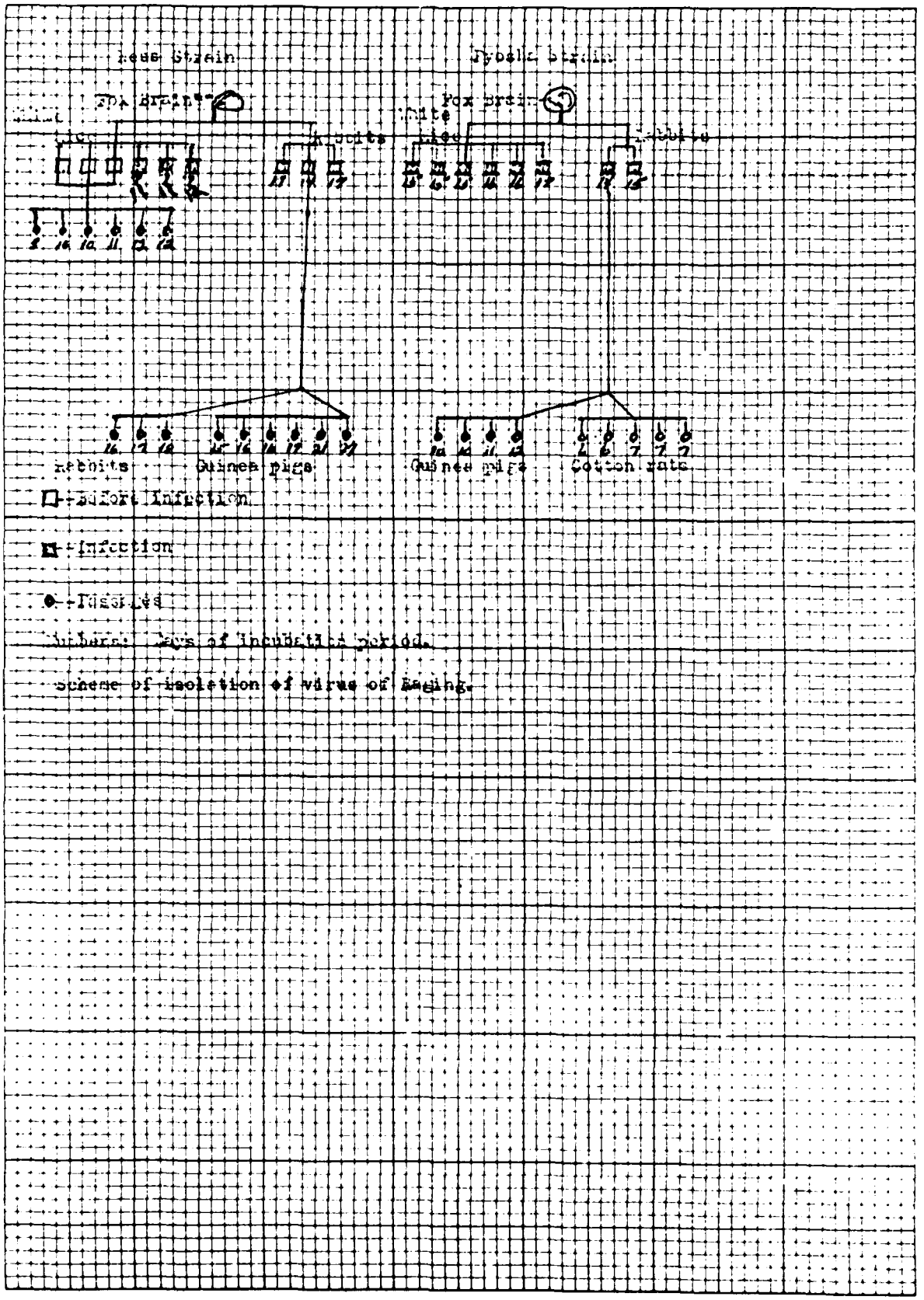

Table 1. Tests on filtering the virus of "Raging" through membrane filters.

No. of filter	5% virus suspension			
	Ness strain		Pyosha strain	
	Test 1	Test 2	Test 1	Test 2
1	4/5	5/5	3/5	4/5
2	4/5	5/5	3/5	3/5
3	4/5	5/5	4/5	5/5
12	5/5	5/5	5/5	5/5
Control	5/5	5/5	5/5	5/5

In all tables: Numerator- number of mice which died; Denominator--number of infected mice.

Table 2. Pathogenicity of virus of Raging for laboratory animals.

Animal	Type of infection	Strain Ness	Strain Pyosha
White mice	Intra-brain	4/4	4/4
	Intra-muscle	3/4	4/4
	Subcutaneous	2/4	1/4
Rabbits	Intra-brain	4/4	4/4
	Intra-muscle	3/4	2/4
	Subcutaneous	1/2	0/2
Guinea pigs	Intra-brain	3/3	3/3
	Intra-muscle	2/3	1/3
	Subcutaneous	1/3	1/3
Cotton rats	Intra-brain	-	6/6

Table 3. Titering of virus of Raging on mice.

Strain	Mode of infection	Dilution of the virus&suspension					
		10-1	10-2	10-3	10-4	10-5	LD50
Ness	Intra-brain	4/4	4/4	4/4	4/4	1/4	1/45700
	Intra-muscle	4/4	1/4	0/4	0/4	0/4	1/45
	Subcutaneous	3/4	0/4	0/4	0/4	0/4	1/21
Pyosha	Intra-brain	4/4	4/4	4/4	2/4	1/4	1/7400
	Intra-muscle	4/4	1/4	0/4	0/4	0/4	1/45
	Subcutaneous	2/4	0/4	0/4	0/4	0/4	1/10

Table 4. Survival of Aging virus in glycerine.

Months storage	Dilution of virus suspension 10-1	
	Strain Ness	Strain Pyosha
2	5/5	5/5
4	5/5	5/5
7	2/5	4/5
9	1/5	3/5

Table 5. Stability of virus of Aging to action of 1% phenol.

Strain	Material studied	Period of inactivation				
		2 wks	1 month	2 months	3 months	4 months
Ness	5% brain Suspension	5/5	3/5	2/5	1/5	0/5
Pyosha	5% brain suspension in 1% phenol	5/5	4/5	3/5	0/5	0/5

Table 6. Effect of ultraviolet radiation on the pathogenic activity of virus of Aging

Strain	Test	Period of exposure in minutes				
		5	10	20	30	Control
Ness	1	0/5	0/5	0/5	0/5	5/5
	2	1/5	0/5	0/5	0/5	5/5
Pyosha	1	1/5	0/5	0/5	0/5	5/5
	2	1/5	0/5	0/5	0/5	0/5

Table 7. Effect of high temperatures on the pathogenicity of virus of Aging

Temperature	Period of heating in minutes	Hess strain		Pyosha strain	
		Test 1	Test 2	Test 1	Test 2
50 C.	30	2/3	2/3	3/3	2/3
	40	0/3	2/3	2/3	1/3
	60	0/3	1/3	0/3	0/3
55 C.	20	0/3	0/3	0/3	0/3
	40	0/3	0/3	0/3	0/3
	60	0/3	0/3	0/3	0/3
60 C.	10	0/3	0/3	0/3	0/3
	20	0/3	0/3	0/3	0/3
	40	0/3	0/3	0/3	0/3
Control	—	3/3	3/3	3/3	3/3